Claims

1. A recombinant *Streptomyces hygroscopicus* host cell that produces 16-desmethyl-27-desmethoxyrapamycin.

2. The compound 16-desmethyl-27-desmethoxyrapamycin in substantially pure form.

3. A recombinant *Streptomyces hygroscopicus* host cell that produces a compound selected from the group consisting of 17,18-dihydrorapamycin, 19,20-dihydrorapamycin, 21,22-dihydrorapamycin, 17,18,19,20-tetrahydrorapamycin, 17,18,21,22-tetrahydrorapamycin, 19,20,21,22-tetrahydrorapamycin, 17,18,19,20,21,22-hexahydrorapamycin, 16-demethyl-17,18-dihydrorapamycin, 16-demethyl-19,20-dihydrorapamycin, 16-demethyl-21,22-dihydrorapamycin, 16-demethyl-17,18,19,20-tetrahydrorapamycin, 16-demethyl-17,18,21,22-tetrahydrorapamycin, 16-demethyl-19,20,21,22-tetrahydrorapamycin, 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, 17-desmethylrapamycin, 23-desmethylrapamycin, 17,23-didesmethylrapamycin, 17-desmethyl-17,18-dihydrorapamycin, 17-desmethyl-19,20-dihydrorapamycin, 17-desmethyl-21,22-dihydrorapamycin, 17-desmethyl-17,18,19,20-tetrahydrorapamycin, 17-desmethyl-17,18.21,22-tetrahydrorapamycin, 17-desmethyl-19,20,21,22-tetrahydrorapamycin, 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 23-desmethyl-17,18-dihydrorapamycin, 23-desmethyl-19,20-dihydrorapamycin, 23-desmethyl-21,22-dihydrorapamycin, 23-desmethyl-17,18,19,20-tetrahydrorapamycin, 23-desmethyl-17,18,21,22-tetrahydrorapamycin, 23-desmethyl-19,20,21,22-tetrahydrorapamycin, 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 17,23-didesmethyl-17,18-dihydrorapamycin, 17,23-didesmethyl-19,20-dihydrorapamycin, 17,23-didesmethyl-21,22-dihydrorapamycin, 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, 19-methylrapamycin, 19,20-del-rapamycin, 18-hydroxyrapamycin, 18-ketorapamycin, and 18-saturated-rapamycin.

4. A compound selected from the group consisting of 17,18-dihydrorapamycin, 19,20-dihydrorapamycin, 21,22-dihydrorapamycin, 17,18,19,20-tetrahydrorapamycin, 17,18,21,22-tetrahydrorapamycin, 19,20,21,22-tetrahydrorapamycin, 17,18,19,20,21,22-hexahydrorapamycin, 16-demethyl-17,18-dihydrorapamycin, 16-demethyl-19,20-dihydrorapamycin, 16-demethyl-21,22-dihydrorapamycin, 16-demethyl-17,18,19,20-tetrahydrorapamycin, 16-demethyl-17,18,21,22-tetrahydrorapamycin, 16-demethyl-19,20,21,22-tetrahydrorapamycin, 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, 17-desmethylrapamycin, 23-desmethylrapamycin, 17,23-didesmethylrapamycin, 17-desmethyl-17,18-dihydrorapamycin, 17-desmethyl-19,20-dihydrorapamycin, 17-desmethyl-21,22-dihydrorapamycin, 17-desmethyl-17,18,19,20-tetrahydrorapamycin, 17-desmethyl-17,18.21,22-tetrahydrorapamycin, 17-desmethyl-19,20,21,22-tetrahydrorapamycin, 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 23-desmethyl-17,18-dihydrorapamycin, 23-desmethyl-19,20-dihydrorapamycin, 23-desmethyl-21,22-dihydrorapamycin, 23-desmethyl-17,18,19,20-tetrahydrorapamycin, 23-desmethyl-17,18,21,22-tetrahydrorapamycin, 23-desmethyl-19,20,21,22-tetrahydrorapamycin, 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 17,23-didesmethyl-17,18-dihydrorapamycin, 17,23-didesmethyl-19,20-dihydrorapamycin, 17,23-didesmethyl-21,22-dihydrorapamycin, 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, 19-methylrapamycin, 19,20-del-rapamycin, 18-hydroxyrapamycin, 18-ketorapamycin, and 18-saturated-rapamycin, in substantially pure form.

5. A recombinant *Streptomyces hygroscopicus* host cell that expresses a hybrid PKS composed of at least a portion of a rapamycin PKS and at least a portion of a heterologous PKS.

6. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue.

7. A recombinant *Streptomyces hygroscopicus* host cell that expresses a PKS composed of only a portion of a rapamycin PKS.

8. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue produced by a hybrid PKS composed of at least a portion of a rapamycin PKS and at least a portion of a heterologous PKS.

9. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue produced by a PKS consisting essentially of only a portion of a rapamycin PKS.

10. The recombinant Streptomyces hygroscopicus host cell of claim 6 in which rapI gene, rapJ, rapM, or rapQ has been deleted or inactivated.

11. The recombinant Streptomyces hygroscopicus host cell of claim 10 in which rapI gene, rapJ, rapM, or rapQ has been deleted or inactivated.

12. The recombinant Streptomyces hygroscopicus host cell of claim 11 in which rapN and rapO have been deleted or inactivated.

13. The recombinant Streptomyces hygroscopicus host cell of claim 12 in which rapN, rapO and rapM have been deleted or inactivated.

14. The recombinant Streptomyces hygroscopicus host cell of claim 13 in which rapM, rapN, rapO, and rapQ have been deleted or inactivated.

15. The recombinant Streptomyces hygroscopicus host cell of claim 14 in which rapL, rapM, rapN, rapO, and rapQ have been deleted or inactivated.

16. The recombinant Streptomyces hygroscopicus host cell of claim 6 that produces 16-desmethyl-27-desmethoxyrapamycin.

17. The recombinant Streptomyces hygroscopicus host cell of claim 6 that expresses a rapamycin PKS derivative in which at least one domain of one module of the is deleted or inactivated, wherein said cells does not comprise a rapamycin PKS derivative that contains a heterologous PKS domain, module, or protein.

18. A method of making a rapamycin analog comprising culturing a host cell of claim 6 under conditions where the analog is produced.

19. The method of claim 18 wherein the rapamycin analog is 16-desmethyl-27-desmethoxyrapamycin.

20. 16-desmethyl-27-desmethoxyrapamycin produced by a method comprising culturing a host cell of claim 16 under conditions where 16-desmethyl-27-desmethoxyrapamycin is produced.